1649-Pos Board B541
Kinesin Walks on Microtubule through the Conformation-Extension Mechanism
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Since its discovery in 1985, Kinesin has attracted extensive interests about its biologic role in cell living. However, it is still a question how kinesin converts chemical energy from ATP hydrolysis to mechanical energy for the movement of cargo. Our hypothesis is that kinesin works through dynamic conformations, which are difficult to capture with x-ray crystallography and electron microscopy. using an advanced simulation method, the self-guided Langevin dynamics (SGLD), we discovered that kinesin has a highly dynamic microtubule binding interface (MTBI). In aqueous solutions, kinesin extends the MTBI motif and forms an extended conformation. In kinesin-microtubule complexes, kinesin has a dynamic conformation and can convert to the extended conformation at high energy levels. Based on these discoveries, we proposed the conformation-extension mechanism for motor proteins. This mechanism opens a new view of motor proteins and explains well many experimental observations.

1650-Pos Board B542
Simulations of Neck Linker Modified and One Head Loaded Kinesin
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Recently, Czovek et al. established a complete, thermodynamically consistent, and still simple kinetic model for the two-headed homodimeric motor protein, kinesin. Computational simulations based on the model verified the essential role of the conformational changes of the polymer chain connecting the two motor domains (neck linkers, NLs) in the directional movement and force-generation of conventional kinesin. The model was able to reproduce a large number of experimental data (speed, dwell time distribution, randomness, processivity, hydrolysis rate, etc.) astonishingly well under normal as well as under highly unphysiological conditions. Moreover, it enabled a more detailed deconvolution of the mechanochemical cycle than it is experimentally possible. Having such a powerful model, we apply it to modified versions of the wild-type kinesin. Our aim is to test how the behavior of the kinesin is affected when i) either the length of the NLs are changed ii) or the pulling force is applied at one of the two motor domains rather than at the stalk.
The comparison of our results with the available experimental data leads to a more detailed understanding of how kinesin operates.

1651-Pos Board B543
Cargo Transport by Kinesins in Viscoelastic Fluids
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Kinesins are dimeric molecular motors which are responsible for intracellular transport. The motion of kinesins and their cargoes has been characterized by in vitro experiments, and several models have been developed for transport in purely viscous fluids. However, previous models are inadequate to predict the effects of viscoelastic fluid on the transport. In this study, a new mechanistic model is proposed to capture the motion of a cargo transported by a single kinesin in a viscoelastic fluid. The proposed model is mechanistic and can also be applied to transport in viscoelastic fluid done by other kinds of molecular motors. A generalized Langevin equation and fractional Brownian motion are used. During the unsteady state, the force induced by elasticity of the fluid changes with the motion of the cargo. As a result, the load acting on the cargo changes with both its displacement and its velocity. This is captured by a memory function which is used in the generalized Langevin equation and contains all past states. The steady state motion is captured by excluding the significantly distant past states from the memory function. Transport velocities were calculated for various ratios between viscosity and elasticity. For highly viscoelastic fluids, the relation between the velocity and this ratio was not monotonic. Also, the velocity is observed to be maximal when the ratio is about 0.5.

1652-Pos Board B544
A Modified Active Brownian Dynamics Model using Asymmetric Energy Conversion and its Application to Cargo Transport by Multi-Motors
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We consider a modified active Brownian particle model for an application to the cargo transport by multi-motors. In our model each motor has its own energy depot to convert the internal energy into mechanical energy via a nonlinear conversion mechanism and is interacting with the cargo harmonically. A different kind of motor is described by a different strength of interaction. By introducing stochastic energy supply to each motor independently and flashing ratchet potential synchronized to the stochastic energy supply, we perform an active Brownian dynamics simulation. Mean velocity, stall force, forward-backward step profiles are investigated for various interaction strengths of the motors with the cargo under the influences of external load, thermal noise, and ATP concentration.

1653-Pos Board B545
Evaluation of Exponential Distributions Measured from Single Fluorescent Molecules
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Characterizing a Poisson process is very important in biology, because most of the underlying processes are influenced by finite on- and off-rates. However, accessing the complete distribution often proves difficult due to limitations in time and spatial resolution. Additionally, the experimental setup often introduces systematic errors, which require correction. Here, we use numerical simulations to estimate the statistical and systematic errors that commonly occur when evaluating exponential distributions obtained from measurements. With regard to measurements on the stepping of fluorescently-labeled motor proteins on cytoskeletal filaments, we additionally test methods to correct for photobleaching and the limited lengths of the filaments. Results of the simulations are compared to experimental data on kinesin-1 motors walking along microtubules. Our work will not only improve the error estimation for experimental data, but will also allow for better statistical comparison of two or more populations of motor proteins (e.g. motors with distinct mutations or motors linked to different cargos).

1654-Pos Board B546
Quantitative Assessment of Single Molecule Motility In Vivo
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In vitro single molecule motility assays allow for the direct characterization of molecular motor properties including stepping velocity and characteristic run length. While application of these techniques in vivo is feasible, the challenges involved in sample preparation as well as the added complexity of the cell and its systems result in reduced ability to collect large datasets, as well as difficulty in simultaneous observation of the components of the motility system, namely motor and track. To address these challenges, we have developed simulations to characterize motility datasets in order to understand data behavior and the effects of undersampling. We introduce the use of a simple bootstrapping technique that allows for the quantification of measurement uncertainty and a Monte Carlo permutation resampling scheme for the measurement of statistical significance and the estimation of required sample size. In addition, we have modeled motility collected in the absence of simultaneous track observation and developed a theoretical framework for the determination of characteristic run length in systems where motility and track length must be characterized sequentially, which shows good agreement with in vitro motility experiments on two kinesin constructs walking on microtubules stabilized by either paclitaxel or the GTP analog GMPCPP.

1655-Pos Board B547
Tau Dynamics on the Microtubule Surface Modulate Kinesin Motility in an Isoform and Lattice Specific Manner
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Tau is a microtubule associated protein known to modulate processive kinesin movement in an isoform and microtubule lattice specific manner (McVicker et al., (2011) J Biol Chem 286:42873). To further investigate the mechanisms by which Tau modulates kinesin motility we have used single molecule imaging techniques to examine the dynamic behavior of both the 3RS- and 4RL-isoforms of Tau on different microtubule tracks, stabilized with either paclitaxel or guanylyl-(α,β)-methylene-diphosphate (GMPCPP), which mimic the GDP- and GTP-states of the microtubule lattice, respectively. We find both isoforms of Tau interconvert between static and diffusing populations on the microtubule surface, and the equilibrium between these two states depends on both the isoform of Tau and the structure of the underlying microtubule lattice. On paclitaxel-stabilized microtubules, we find 3RS-Tau favors the static conformation and forms complexes consisting of 2-3 molecules, while 4RL-Tau predominantly exists as a single molecule equally distributed between the static and diffusing populations. However, on GMPCPP-stabilized microtubules both isoforms of Tau favor the diffusing conformation and do not form static complexes composed of more than one molecule. These results explain both the